Resolution of Lipohypertrophy Following Change of Short-acting Insulin to Insulin Lispro (Humalog®)

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Lipohypertrophy as a local complication of insulin therapy is well recognized. Despite improvements in insulin purity and the introduction of recombinant human insulin its prevalence has remained high. Rotation of injection sites can reduce the frequency of the problem but does not abolish it. The importance of this complication is not only cosmetic but also in its impact on insulin absorption, and hence glycaemic control. We report a patient who had intractable lipohypertrophy with human recombinant insulin but experienced no such problem when converted onto the insulin analogue lispro. We suggest that the faster speed of absorption of insulin lispro may lead to less hypertrophic stimulation of subcutaneous adipocytes. This difference may be clinically useful in susceptible individuals. © **1998 John Wiley & Sons, Ltd.**

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Introduction

Lipodystrophy is a recognized local complication of insulin therapy. Improvements in the purity of insulin preparations and the widespread use of recombinant human insulin have dramatically reduced the prevalence of lipoatrophy, but the prevalence of lipohypertrophy has been little affected, with reported incidences of up to 30 %.[1–3] Rotation of injection sites can reduce the frequency of lipohypertrophy but does not abolish it. The occurrence of this complication has cosmetic importance and can affect insulin absorption[4,5] and, by implication, glycaemic control. Lipohypertrophy therefore remains a challenge to the clinician and can be a major disability in the susceptible individual.

Case Report

A 23-year-old male was diagnosed as having Type 1 diabetes mellitus in February 1977 when he was $3\frac{1}{2}$ years of age. There was no significant past medical history, he had no other illnesses, and there was no family history of diabetes. At diagnosis he was started on 4 U soluble insulin b.d. and progressed well. His care was transferred from his paediatricians in August 1987, at which time he was taking Human Actrapid® (Novo Nordisk, Pease Pottage, UK) (14 U am, 11 U pm) and Human Monotard® (Novo Nordisk, Pease Pottage, UK) (28 U am, 8 U pm). His glycaemic control was good, HbA_{1c} 6.5 % (non-diabetic range 3.6–6.2 %) and he had no evidence of end organ complications. His injection sites were normal.

In February 1988 he complained of lipohypertrophy. He was advised on rotation of injection sites. His glycaemic control at this time had deteriorated with fluctuating home blood glucose recordings. In January 1989 his insulin was changed to three times a day human Actrapid® given via Novopen® (Novo Nordisk, Pease Pottage, UK), with nocte Ultratard® (Novo Nordisk, Pease Pottage, UK). His HbA_{1c} at this time was 8.4 % (non-diabetic range 3.2–6.4 %).

During the next 7 years his attendance at follow up was irregular. When seen in 1990 there were concerns about loss of hypoglycaemic awareness and he changed temporarily to pork Velosulin® (Novo Nordisk, Pease Pottage, UK) from human Actrapid® By 1992, he had reverted to his previous insulin regime. When he re-attended for follow-up in 1996 his glycaemic control was markedly worse, with HbA_{1c} of 10.8 % (non-diabetic range 4.7–6.4 %). He had also developed background retinopathy and intermittent proteinuria. His previously noted lipohypertrophy was markedly worse, particularly on his arms and legs. He was advised to inject only in his buttocks and abdomen and to rotate sites regularly.

At his next visit, lipohypertrophy had occurred at these sites also. His glycaemic control was no better and his hypoglycaemic awareness remained impaired. It was decided to change his short-acting insulin to insulin

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lispro (Humalog® Eli Lilly, Hampshire, UK). At his next visit he reported no further lipohypertrophy and some resolution at the previously affected areas. The fluctuations in his home blood glucose monitoring seemed to improve, although HbA_{1c} remained unchanged. His night time Ultratard® was changed to Insulatard® (Novo Nordisk, Pease Pottage, UK) at this point. When last seen in February 1997 he was well, with no new areas of lipohypertrophy and continued resolution at previously affected areas. His glycaemic control was improving with an HbA_{1c} of 9.6 %. He has since moved from the area.

Discussion

In the case described, lipohypertrophy was a significant problem. It caused the patient considerable distress due to the change in his appearance. The period when the lipohypertrophy was most noticeable corresponded to the period when glycaemic control was at its worst and most variable. Given the subject's limited hypoglycaemic awareness this variability of blood glucose was a significant problem. As lipohypertrophy has been shown to affect insulin absorption[4,5] it is possible that this contributed to this variability in blood glucose.

The marked improvement in lipohypertrophy when changed onto insulin lispro was prompt and sustained, and occurred in the absence of any other changes in treatment or injection technique. This implies that, in this individual at least, the improvement was probably due to insulin lispro not providing the same lipohypertrophic stimulus as soluble human insulin. This effect is biologically plausible, as the insulin lispro molecule is structurally different from human insulin. In particular, insulin lispro is absorbed more rapidly from subcutaneous tissue, as it spends less time in polymeric forms after injection.[6] Therefore the subcutaneous adipocytes will spend less time exposed to the local lipogenic action that insulin has been described to exert.[7] We suggest that this possible difference in the properties of insulin lispro from soluble human insulin may be clinically important in susceptible patients. This warrants further study.

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